

B2 improves skeletal muscle protein kinetics in said individual as compared to individual without said treatment.

B2 Please amend claim 9 as follows:

8/ (twice amended) A method of treating an individual having a severe burn, comprising the step of administering to said individual a pharmacologically effective dose of propranolol, wherein treatment with said propranolol improves skeletal muscle protein kinetics in said individual as compared to individual without said treatment.

#### REMARKS

##### Amendment

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

### The 35 U.S.C. §102 Rejection

Claims 1-13 were rejected under 35 U.S.C. §102(b) as being anticipated by **Herndon** et al. The rejection is respectfully traversed.

Claims 1 and 9 have been amended to recite methods of treating an individual having a severe burn, wherein said treatment with beta-adrenergic antagonist or propranolol improves skeletal muscle protein kinetics in said individual as compared to individual without said treatment. The present invention discloses “ $\beta$  blockade improved skeletal muscle protein kinetics. Propranolol administration improved muscle protein net balance from baseline ( $p=0.005$ ) and as compared with non-treated controls ( $p=0.001$ ) (Figure 2)” (page 23, lines 9-13). Using stable isotope methodology and serial body composition scanning, the present invention shows for the first time that  $\beta$  blockade with propranolol diminishes skeletal muscle protein wasting seen after severe burn (page 28, Discussion; Figure 2 and Table 3). Out of twenty-five severely burned children studied, thirteen were safely given propranolol and experienced a decrease in resting energy expenditure. Twelve had

improved net muscle protein balance. With long-term  $\beta$ -blockade, this translated into greater lean body mass.

In contrast, **Herndon** et al. taught "selective  $\beta_1$ -adrenergic and nonselective adrenergic receptor blocking agents can significantly reduce heart rate and myocardial oxygen consumption in hypermetabolic burned patients without adversely affecting protein kinetics" (page 1304, left column, last paragraph). **Herndon** et al. did not teach or suggest treatment with beta-adrenergic antagonist or propranolol can improve skeletal muscle protein kinetics in treated individual as compared to untreated individual as claimed herein.

Furthermore, **Herndon** et al. actually teach away from the present invention because **Herndon** et al. concluded that beta-adrenergic antagonist or propranolol had no effect on muscle protein metabolism in burned patients. **Herndon** et al. reported that

"in the present study, we failed to document an effect of propranolol and metoprolol on protein kinetics, although an earlier study indicted an increase in urea production with propranolol. ....in the present study, we used two independent approaches of assessing net protein

breakdown. The fact that neither of these techniques revealed any significant effect of either agent on protein kinetics indicates that the effect is of minimal clinical concern. In summary, selective  $\beta$ 1-adrenergic and nonselective adrenergic receptor blocking agents can significantly reduce heart rate and myocardial oxygen consumption in hypermetabolic burned patients without adversely affecting protein kinetics." (page 1304, left column, second and third paragraphs).

Therefore, based on the teaching of no effect on protein kinetics disclosed in **Herndon** et al., the instant finding of improved skeletal muscle protein kinetics in individual treated with beta-adrenergic antagonist or propranolol is an unexpected result.

In view of the above remarks, **Herndon** et al. did not teach or suggest each and every aspect of the instant invention. Instead, **Herndon** et al. teach away from the present invention. Hence, **Herndon** et al. did not anticipate claims 1 and 9 of the instant application. Accordingly, Applicant respectfully requests that the rejection of claims 1-13 under 35 U.S.C. §102(b) be withdrawn.

This is intended to be a complete response to the Office Action mailed June 19, 2002. If any issues remain outstanding, the Examiner is respectfully requested to telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claim 1 has been amended as follows:

1. (twice amended) A method of treating decreasing ~~muscle protein catabolism~~ in an individual having a severe burn, comprising the step of administering to said individual a pharmacologically effective dose of a beta-adrenergic antagonist, wherein treatment with said beta-adrenergic antagonist improves skeletal muscle protein kinetics in said individual as compared to individual without said treatment.

Claim 9 has been amended as follows:

9. (twice amended) A method of treating decreasing ~~muscle protein catabolism~~ in an individual having a severe burn, comprising the step of administering to said individual a pharmacologically effective dose of propranolol. wherein treatment with said propranolol improves skeletal muscle protein kinetics in said individual as compared to individual without said treatment.



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